

2019-08-15

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<http://hdl.handle.net/10026.1/14812>

10.1002/mdc3.12831

Movement Disorders Clinical Practice

Wiley

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**Title: Lower limb somatosensory discrimination is impaired in people with Parkinson's disease:
novel assessment and associations with balance, gait and falls.**

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Word Count: Main text: 3556; Abstract: 250

Running title: Somatosensory discrimination in Parkinson's disease

Key words: Parkinson's disease, somatosensory, outcome measure, lower limb, mobility

Abstract

Background: People with Parkinson's disease (PD) often have compromised walking and balance. This may be due to impaired lower limb tactile and proprioceptive sensation. Existing clinical measures may not be sufficiently sensitive to uncover these sensory impairments.

Objective: Determine whether novel measures of lower limb somatosensory discrimination are psychometrically robust and associated with mobility outcomes in people with PD.

Methods. Lower limb somatosensation was assessed on two occasions, 3-7 days apart, using three novel tests: gradient discrimination, roughness discrimination, and step height discrimination. Static and dynamic balance (Brief Balance Evaluations Systems Test), falls incidence, falls confidence (Falls Efficacy Scale), gait (speed and step length) were also obtained. Participants were twenty-seven people with PD and twenty-seven healthy controls (HC).

Results: Novel tests showed good-excellent intra-rater reliability ($ICC=0.72-0.92$). Significantly higher gradient and step height discrimination thresholds ($p<0.01$) were demonstrated in PD compared to HC, indicating worse position sense at the ankle, knee and hip. Significant correlations were identified between gradient discrimination and falls incidence ($r=0.55$), falls confidence ($r=0.44$), balance ($r=0.63$), but not gait ($r=0.21$). Step height discrimination was significantly correlated with balance ($r=0.54$). Foot roughness discrimination was not significantly different between people with PD and HC and was not significantly correlated with mobility measures ($p>0.05$).

Conclusion: These novel tests are psychometrically robust and identify impaired lower limb position sense which were associated with balance and falls in this sample of PD. Interventions targeting somatosensory processing in PD may improve aspects of balance and reduce falls risk. Further research is warranted.

Introduction

Parkinson's disease (PD) is the second-most common neurodegenerative disease after dementia.¹ It is a progressive neurological condition characterised by both motor and non-motor symptoms with many clinical symptoms related to difficulties with movement. Such difficulties often lead to postural instability, reductions in walking ability and impaired balance which negatively impact participation in activities of daily living, quality of life and falls.^{2,3}

The view that movement difficulties in people with Parkinson's disease (PD) are attributable purely to motor deficits has been challenged in recent years by evidence of impaired processing and integration of somatosensory information⁴. Tactile and proprioceptive sense, referred to as somatosensation, arise from sensory receptors in skin, joints, tendons, and muscles providing feedback of an individual's body position, body and limb motion, and interaction with the environment.⁵ Studies have shown people with PD to have deficits in somatosensory processing such as elevated thresholds to spatial and temporal stimuli,⁴ diminished proprioceptive and position sense awareness,^{6,7} and impaired haptic sensation.⁸ Moreover, when visual feedback cannot be used, people with PD lack precision in their stepping,⁹ show greater errors in obstacle clearance,¹⁰ and have greater difficulty controlling postural orientation on the basis of available somatosensory and vestibular information compared to healthy controls¹¹. Unsurprisingly, deficits in lower limb proprioception are significantly associated with falls incidence in people with PD.⁷ It is feasible to posit that sensory deficits may contribute to many of the movement and balance difficulties which are the hallmark of PD. Accurately identifying and quantifying the severity of lower limb somatosensory abnormalities and, crucially, how they are associated with activity and participation limitations represents an important goal to inform rehabilitation interventions.

Several measures of somatosensory function have been evaluated and reviewed¹² in neurological populations, with the Erasmus MC modified Nottingham Sensory Assessment (EmNSA)¹³, and the sensory scale of the Fugl-Meyer Assessment¹⁴ suggested to provide the best balance of clinical utility and psychometric robustness¹². Those measures, however, have been widely criticised for largely assessing the detection of stimuli - the lowest level of sensory processing¹⁵, not

79 providing functionally meaningful somatosensory data, and being insufficient for uncovering the
80 complexities of somatosensory perception^{4,16,17}. Furthermore, they have not been evaluated in people
81 with PD. A recent review of proprioception assessment methods¹⁸ highlights a concerning paradox:
82 measures which possess clinical utility lack accuracy, whilst those which possess accuracy lack
83 clinical utility. More complex tests of tactile sensation and proprioceptive function such as matching
84 one or more standardised sensations to another, integrating sensation with motor output or
85 distinguishing the temporal or spatial qualities of two stimuli have been shown to uncover
86 somatosensory dysfunction in Parkinson's, yet are largely limited to the laboratory setting.^{4,6} In
87 response to the perceived shortcomings of existing clinical measures, we developed three novel and
88 functionally oriented tests of somatosensory discrimination: the Foot Roughness Discrimination Test
89 (FoRDT™), the Step height Discrimination Test (StepDT™) and the Gradient Discrimination Test
90 (GradDT™). These functionally oriented tests have been described and evaluated previously in a
91 stroke population^{19,20} showing superior psychometric properties to the clinically feasible and
92 psychometrically robust sensory measure the Erasmus MC modified version of the Nottingham
93 Sensory Assessment (EmNSA).¹³ To date, however, our novel tests have not been evaluated in people
94 with PD.

95 The aim of this study was to evaluate the psychometric properties of these novel somatosensory
96 measures in people with PD, and report on their associations with clinical measures of gait, balance
97 and falls. Specific objectives were to evaluate intra-rater reliability of the novel measures and
98 convergent and known-group validity. Further, we wished to explore the association between our
99 novel measures with functional measures of gait, balance and falls in people with PD.

100 Method

101 Participants

102 We recruited a convenience sample of 27 people with PD and 27 age matched healthy
103 controls. People with PD were identified through local branches of Parkinson's UK (a UK charity)
104 and healthy age matched controls were recruited through the University of the 3rd Age (a UK

volunteer-led organisation providing educational and leisure opportunities to retired/semi-retired individuals). Inclusion criteria were: ability to provide informed consent, walk 10 meters unsupervised (with or without a walking aid), have no have significant cognitive impairment ($\geq 24/30$ Mini Mental State Examination, MMSE)²¹ or comorbidities known to affect somatosensation (e.g. diabetic neuropathy). Age matched control participants were included providing they had no pathological conditions known to affect balance, mobility or sensation. Sample size calculations²² indicated a sample size ≥ 27 per group was sufficient for: a 95% CI of 0.25 and a planned ICC of 0.8 ($\alpha=0.05$); detecting a correlation coefficient of 0.29 (power=0.85, $\alpha=0.05$); and effect size of 0.79 (power=0.85, $\alpha=0.05$).

Procedures

Ethical approval was obtained from the University of Plymouth, Faculty of Health and Human Sciences Research Ethics Committee (ref: 17/18-86). People with PD (n=27) were tested with the novel sensory measures on two occasions, between 3-7 days apart at the same time of day and in their self-reported ON state; that is the state in which they felt they were optimally responsive to their medication. The first author was the rater on test session 1 and test session 2. Control participants (n=27) were tested with the novel measures on just one occasion.

Participant demographic characteristics (age, gender) and in the case of people with PD, time since diagnosis, upper and lower limb motor function (Movement Disorder Society - Unified Parkinson's Disease Rating Scale motor score Part III (MDS -UPDRS III)²³ was collected. Alongside the somatosensory tests a range of different health constructs were measured, described below.

Outcome measures:

The *EmNSA*¹³ was used to determine convergent validity of our novel tests. It is considered to be a psychometrically robust and clinically feasible assessment tool¹² involving the assessment of exteroceptive sensation (light touch, pressure touch, and pin-prick), higher cortical discriminatory sensation (sharp-blunt) and proprioception (movement detection and discrimination).

The *Gradient Discrimination Test (GradDT™)* evaluates sensory-perceptual ability to discriminate underfoot surface gradient or slope during standing. It has been described previously and shown to be reliable and valid in a stroke population.²⁰ It utilises a two alternative forced choice paradigm (2AFC),²⁴ in which two differing sloping platforms, a base and a comparator, are mentally compared (discriminated). The test procedure involves participants standing on a series of adjustable sloping platforms until a discrimination threshold is reached (i.e. the point at which the participant cannot discriminate between two different slopes). This provides a discrimination threshold in degrees (°). The test takes 7-10 minutes to complete.

The Step height Discrimination Test (StepDT™) utilises the 2AFC approach as detailed above and has been described and psychometrically evaluated previously in stroke.²⁰ This test assesses an individual's ability to discriminate the height of a step, through lower limb position sense, without visual feedback. The test involves the passive placement of the test limb onto a series of adjustable steps. The 2AFC test procedure involves increasingly difficult trials until the point at which the individual cannot consistently discriminate which of the two presented steps is highest. This provides a discrimination threshold in centimetres (cm).

The Foot Roughness Discrimination Test (FoRDT™), described and evaluated previously,¹⁹ assesses haptic tactile sensory ability of the plantar aspect of the foot. It comprises a series of textured foot plates, each with standardised and quantifiable gratings. The test involves the haptic exploration of underfoot textured plates in a series of increasingly difficult trials until a roughness discrimination threshold is reached (i.e. the point at which the participant cannot discriminate between two textures). The gratings are expressed as spatial intervals (i.e. the distance between measured in micrometres (µm) ($1\mu\text{m} = 1/1000$ millimetre (mm))). The larger the spatial interval, the rougher the surface is perceived to be up to a point of between 3000 -3500µm.²⁵ This provides a roughness discrimination threshold in micrometres (µm).

These discrimination tests are undertaken with the participant in standing to reflect, as near as possible, "real life" foot-ground sensorimotor interactions. Upper limb support was provided for safety and to aid participants with balance/weight transfer. Participants were requested to look straight

ahead and avoid looking down at their feet during the testing procedure. In each test, a greater discrimination threshold indicates worse somatosensory ability.

Measures of balance, gait and falls

The *Brief Balance Evaluation Systems Test (Brief BESTest)*²⁶ is an eight item test, developed from the original BESTest,²⁷ and assesses six subsystems of static and dynamic balance control: biomechanical constraints, stability limits/verticality, anticipatory postural responses, postural responses, sensory orientation, and stability in gait. Administration time is less than 10 minutes, making it feasible to use in clinical practice, whilst concurrent and convergent validity has been demonstrated in individuals with Parkinson's disease.²⁸

The *10 metre Walk Test (10mWT)*²⁹ was used to assess gait speed (comfortable walking speed using a rolling start) and stride length calculated in metres per second and steps per metre respectively. The 10mWT is recommended for use in assessing gait speed in PD.³⁰

Falls Incidence. Falls data was collected through participant retrospective recall over the previous three month period. This is recommended as a simple, and effective starting point for establishing falls history.³¹ We used a well-accepted definition of falls: 'an unexpected event in which the participant comes to rest on the ground, floor, or lower level'³²

Fear of falling. Fear of falling was measured using the *Falls Efficacy Scale - International (FES-I)*³³ a 16-item self-report tool, which measures an individual's level of concern about falling during social and physical activities inside and outside the home. Higher scores indicate greater fear of falling, which is associated with future falls, activity limitations and reduced quality of life in PD.³⁴

Statistical analysis

Statistical analyses were performed using SPSS version 22.0. Data were summarised using frequencies and percentages, mean and standard deviation (SD) or median and inter-quartile range (IQR) as appropriate. Data distribution was assessed for normality using Shapiro-Wilks tests and assumed normally distributed when $p > 0.05$. Data presented for the GradDT™, StepDT™ and

FoRDT™ represent discrimination thresholds expressed in the original measurement units. Larger discrimination thresholds indicate worse sensory function.

Necessary assumptions in reliability testing were accounted for which included stability between testing sessions of participant sensory function and consistency in the testing situation (environment, test procedure, medication and time of day). Intra-rater reliability were analysed using Intra class Correlation Coefficient (ICC_{2,1}) in line with the Guidelines for Reporting Reliability and Agreement Studies (GRRAS).³⁵ Standard error of measurement (SEM) provided an indication of the score likely due to measurement error. Coefficient of repeatability (CoR), a measure of absolute reliability provided a score change (in the original measurement scale), which included random and measurement error and so any score above CoR reflects true/real change or smallest real difference.³⁶ It was calculated by multiplying the SEM by 2.77 ($\sqrt{2} \times 1.96$).³⁶

Sensory performance of the lower limbs of people with PD and matched healthy controls allowed for an evaluation of known group validity. A Mann Whitney U test was used to determine statistical significance between the groups ($p < 0.05$) as data for each sensory measures was not normally distributed. Effect size (Cohen's d) was calculated to show the size of any difference, using a standardised formula³⁷ and interpreted using Cohen's³⁸ criteria of 0.1 = small effect, 0.3 = medium effect and 0.5 = large effect. Convergent validity was evaluated by comparing our novel tests with the EmNSA with the magnitude of the relationship determined using a Spearman's rank order correlation. The magnitude of the relationship between our novel measures of somatosensation and measures of gait, falls and dynamic balance were evaluated using Spearman and Pearson correlational analysis where appropriate. Strength of correlations were interpreted using the classification where ≤ 0.29 = weak, 0.30- 0.49 = moderate and, ≥ 0.50 = strong.³⁸

Results

Demographic and clinical characteristics: Fifty-four people, 27 people with PD (mean age 71 +/- 5.8 years, male/female = 19/8, and 27 age matched healthy adults (mean age 70 +/- 7 years, male/female = 17/10) were recruited. Parkinson's participants had a mean Movement Disorder

Society - Unified Parkinson's Disease Rating Scale motor score (MDS-UPDRS III) of 30.11 +/- 14.7 (Table 1)

Intra-rater reliability: Test-retest reliability of the novel measures is shown in table 2. Good to excellent mean ICC values were demonstrated in each novel test (ICC =0.72-0.92). Wide 95% confidence intervals in the foot roughness and step height discrimination tests were demonstrated. Coefficient of repeatability scores (i.e. random and measurement error) in the GradDT™ represented 37% of baseline score, 68% in the FoRDT™ and 55% in the StepDT™. Higher scores represent larger random and measurement error. *Known Groups Validity:* People with PD performed worse on sensory measures compared to healthy controls, indicating worse somatosensory function in the lower limbs (Table 3). A Mann Whitney U test revealed significant differences in gradient discrimination thresholds of PD (median=2.5°) and healthy controls (median =1.4°, U=179, z=-3.86, p<0.001, r=.52). Foot roughness discrimination thresholds in PD (median 400µm) whilst higher than healthy controls (median =300µm) were not significantly different (U=353, z=-1.207, p=0.22, r=0.16). Step height discrimination thresholds were significantly different between PD (median =1.8cm) and healthy controls (median=1.2cm, U=209, z=-3.478, p=0.001, r=0.47). EmNSA tactile sensation scores in PD (median =64) were not significantly different from healthy controls (median =62, U=399, Z=-0.533, p=0.59, r= 0.07). EmNSA proprioception scores were also not significantly different between people with PD (median =16) and healthy controls (median =16, U=392, z=-1.013, p=0.31, r=0.13).

Using the EmNSA sensory measure, 55% of people with PD (n=15/27) scored the maximum score (64/64) on tactile sensation component (range 49-64). In the proprioception component of the EmNSA, 81% (n=22/27) of people with PD scored maximally (i.e. 16/16); comparable to healthy control performance (88%, n=24/27). In the novel measures, no single person with PD nor control participant scored the maximum or minimum.

Convergent validity: To evaluate convergent validity, strength of associations between the novel measures and an existing measure of tactile and proprioceptive sensation, the EmNSA were evaluated (table 4). The Foot Roughness discrimination test (FoRDT) showed moderate and significant inverse correlation (r=-0.45, p<0.05) with the tactile component of the EmNSA. As tactile

discrimination thresholds increased, scores on the EmNSA fell, indicating worse tactile sensation. No other significant correlations were demonstrated between our novel measures and the tactile or proprioception components of the EmNSA ($r=0.11-0.28$, $p>0.05$).

Associations between novel measures and balance, gait and falls: Gradient discrimination as measured with the GradDT™ showed the strongest correlations with functional measures of falls and balance (table 5). A significant and strong inverse relationship between the GradDT™ and BriefBESTest ($r=-0.63$, $p<0.01$) indicates that those with higher gradient discrimination thresholds (i.e worse position sense) had lower scores on the BriefBESTest (i.e worse balance performance). The GradDT™ also showed a strong positive correlation with falls incidence and moderate correlation with the Falls Efficacy Scale – International (FES-I), indicating that those with worse gradient discriminative ability reported more falls ($r=0.55$, $p<0.01$) and had greater concerns about falling ($r=0.44$, $p<0.05$). No significant associations between any sensory measure and spatial or temporal aspects of gait were demonstrated.

Discussion

In this study, we evaluated three novel tests of lower limb somatosensory function in a cohort of people with PD and healthy age matched control participants. The sensory-perceptual ability to discriminate surface gradient or slope was assessed during full weight-bearing using the GradDT™. Discrimination of step height using lower limb position sense was assessed with the StepDT™, and the ability to discriminate underfoot surface roughness was evaluated using the FoRDT™. Our study results provide preliminary evidence to support the reliability and validity of these tests in people with PD, and demonstrate people with PD to have impaired lower limb somatosensory discrimination. Moreover, these deficits are associated with worse static and dynamic balance, greater falls incidence and fear of falling.

Our novel measures target key sensorimotor functions related to stance and stepping and use a robust psychophysical testing approach to establish somatosensory discrimination thresholds, i.e. the ability to discriminate the spatial qualities (roughness/gradient/step height) of a stimulus. In contrast

to the more traditional, manual method of assessing lower limb movement detection and direction (i.e. the proprioceptive component of the EmNSA), our weight-bearing tests of gradient discrimination (GradDT™) and step height discrimination (StepDT™) highlighted increased somatosensory discrimination thresholds in people with PD and found these deficits had moderate to strong significant correlations with balance, reported falls and concern about falling. In line with our findings, elevated somatosensory discrimination thresholds to temporal stimuli (STDT), that is, the shortest time interval required for two tactile stimuli to be perceived as separate, have also been found in people with PD compared to healthy controls. Elevated discrimination thresholds at the finger and face³⁹ and toe⁴⁰ have been identified in PD, and have mostly been observed to be correlated with movement performance⁴¹; our findings lend further support to the presence of somatosensory dysfunction in people with PD, and its impact on movement performance, movement function and sensorimotor integration.

Movement and balance are reliant on a complex interaction between sensory and motor systems⁴² whilst the central processing of sensory information ensures the production of a motor plan for task execution that is appropriate to the sensory environment.⁴³ In PD it is postulated that deficits of central processing of somatosensory information, rather than pathology of the peripheral nervous system result in altered integration of sensory and motor information^{4,44} and in particular proprioceptive information⁴⁵. An important function of the dorsal striatum within the basal ganglia (one of the main channels of information processing) is suggested to be the treatment of sensory and motor information coming from the sensorimotor cortex and integrating visual and proprioceptive information onto the motor command.⁴⁶ Using methods which target the integrity of these central processes and the perceptual constructs they sustain may be better achieved by sensory measures which assess discriminative perception rather than simple touch or movement detection. Our data suggest our lower limb novel measures may be better suited to capturing the complexity of somatosensory dysfunction in PD compared to an existing, widely used clinical measure.

That our novel measures of gradient discrimination and step height discrimination were only weakly correlated with the proprioceptive component of the EmNSA suggests they may be measuring

different constructs. This may, at least in part, be accounted for by the fact that the EmNSA assessed proprioception with the participant in supine/sitting, in contrast to our novel measures which assessed position sense with the participant standing in full weight-bearing. Sense of position and sense of movement have also been shown by others to only weakly correlate⁴⁷ which may further help to explain this finding.

The presence of plantar tactile sensory dysfunction in people with PD was not evident in this study as neither tactile scores of the EmNSA nor discrimination thresholds to roughness perception (FoRDT™) were significantly different from healthy controls. Furthermore, tactile plantar sensation as measured by the FoRDT™ did not significantly correlate with our mobility outcomes. Current evidence pertaining to the presence of plantar tactile sensory deficits in people with PD is equivocal^{4,48} with contrasting results explained by variations in study sample characteristics such as disease stage, symptom severity and sensory assessment methods. That most participants in our study were in the early-moderate stages of PD (mean Hoehn & Yahr stage =2.3; time since diagnosis =5.7 years) suggests that reported plantar tactile sensory changes may not occur in early PD. We also recognise the complex and multifactorial nature of balance impairment in PD and the involvement of several ‘systems’ in addition to the somatosensory system²⁷ and so factors other than plantar tactile deficits may also contribute to balance deficits. Nonetheless, that significant deficits of plantar sensation were not evident in our sample, yet proprioceptive deficits were, supports the potential for interventions targeting the plantar aspect of the foot to enhance lower limb position sense/proprioception.

Our study supports that diminished position sense awareness of the lower limbs may also contribute to an increased risk of falls. The strong and significant correlations between lower limb position sense as measured with the GradDT™ and StepDT™ falls incidence and falls confidence indicates worse position sense awareness of the lower limb is significantly associated with more falls and greater fear of falling. This is in line with the findings of others who have found greater error performance and variability in judging obstacle heights when relying on lower limb proprioception¹⁰ which may contribute to an increased risk of trips; and that people with PD who fall have significantly

worse lower limb proprioception, compared to those who don't fall.⁷ The link between falls and lower limb proprioceptive impairment has also been identified in other clinical populations.^{16,49}

Neither temporal nor spatial aspects of gait, as measured by straight line gait speed and number of steps, respectively, were significantly associated with lower limb somatosensory function. Similar findings have been identified in previous studies of healthy and neurological populations^{16,50} and explained by the increased use or sensory weighting of visual information during walking tasks, which may reduce the need for accurate somatosensory information from the lower limbs. In essence, 'simple' straight line gait tasks may be completed using minimal somatosensory information and processing as visual feedback compensates. EEG studies,^{51,52} demonstrate that more complex gait tasks, such as uphill walking and narrow beam walking result in increased activation within somatosensory cortical regions compared with simple straight line gait tasks on the flat, suggesting a greater role for somatosensory information during more complex walking tasks.

Intra-rater reliability was excellent in the GradDT™ although wide reliability confidence intervals and substantial coefficient of repeatability scores for the FoRDT™ and StepDT™ highlight the occurrence of random and/or measurement error. Reliability is an issue in sensory assessments particularly in neurological populations¹² and whilst we attempted to control for random and measurement error, we postulate that the effect of fluctuations in participant energy levels, fatigue and possibly attention, may account for this. The clinical implication is that somatosensory function in people with PD, as with other symptoms, may not be established through one-off assessments, but should be assessed on several occasions in order to gain a true picture. Nonetheless, our novel measures have demonstrated to have distinct advantages over existing measures of lower limb sensation in that they employ an interval level of measurement and show, in this sample, no floor or ceiling effects. The SEM and CoR data provide an indication of random and measurement error which enables interpretation of the true change in scores. Because the CoR is quantified in the same units as the assessment tool, it lends itself for easy clinical interpretation, and can be used to guide decision making. A change in discriminative ability in the gradient test of +/- 0.85° for example, would

indicate change beyond random and measurement error; critical for the monitoring of disease progression and the evaluation of interventions.

This study has several limitations. The testing of discriminative ability places demands on cognitive functions such as attention and working memory; functions which are known to be affected in PD⁵³ and may be further confounded by fatigue and/or motivation.⁵⁴ Formal assessment of fatigue or motivation was not undertaken in this study, so the extent to which it influenced test outcome cannot be determined. We also did not run separate analysis on the effect of lower limb tremor or dyskinesia on somatosensory performance so cannot rule out the impact of these symptoms as our novel tests were designed to reflect ‘real life’ foot-ground sensorimotor interactions during weight-bearing. A further limitation relates to the generalisability of our findings. Our sample was comprised of people in the mild to moderate stages of PD who were tested during the ‘ON’ phase, and so the results may not generalise to those in the more advanced stages of the disease, nor reflect somatosensory function during the ‘OFF’ phase.

Conclusion

To develop targeted and appropriate rehabilitation interventions for people with PD, the recognition that lower limb sensation informs movement and balance function is critical. Key to this is the availability and use of appropriate, clinically feasible and psychometrically robust assessment tools. The development and use of sensory measures which are more closely aligned with the complex sensory-motor function of the lower limb, such as the novel measures evaluated in this article, may enhance understanding in this relatively understudied area of PD. It is hoped that this study provides further insight, and generates discussion into recognising the importance of evaluating somatosensory ability, its relevance to movement, and its rehabilitation in this clinical population.

Acknowledgments

We would like to thank all of the individuals who participated in this study. In particular, Parkinson’s UK North Devon branch members and the University of the 3rd Age, for their help with recruitment. We would also like to thank Dr Kielan Yarrow for his input regarding the methodology of this study.

Author Roles

1. Research project: A. Conception, B. Organization, C. Execution;
2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique

T.G.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B

J.F.: 1A, 2C, 3B

J.M.: 2A, 3B

Disclosures

Funding Sources and Conflict of Interest: No specific funding was received for this work. The authors declare that there are no conflicts of interest relevant to this work.

Financial Disclosures for the previous 12 months: The authors declare that there are no additional disclosures to report.

Ethical Publication Guidelines Statement: This study was conducted in accordance with the University of Plymouth, Faculty of Health and Human Sciences Research Ethics Committee (ref: 17/18-86). Written informed consent was gained from each participant prior to taking part in this study and documented. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

References

1. Pringsheim T, Jette N, Frolkis A, Steeves TD. The prevalence of Parkinson's disease: a systematic review and meta-analysis. *Mov Disord* 2014; 29: 1583–90.
2. Schenkman M, Ellis T, Christiansen C, et al. Profile of functional limitations and task performance among people with early- and middle-stage Parkinson disease. *Phys Ther*. 2011;91:1339–1354.

3. Corallo F, De Cola MC, Lo Buono V, Di Lorenzo G1, Bramanti P1, Marino S. Observational study of quality of life of Parkinson's patients and their caregivers. *Psychogeriatrics*. 2017 Mar;17(2):97-102.
4. Conte A, Khan N, Defazio G, Rothwell J, & Berardelli A. Pathophysiology of somatosensory abnormalities in Parkinson disease. *Nature Reviews: neurology*. 2013;12; 687-697
5. Proske U & Gandevia S. The proprioceptive senses: their roles in signalling body shape, body position and movement, and muscle force. *Physiol Rev* 2012; 92: 1651–1697
6. Teasdale H, Preston E & Waddington G. Proprioception of the ankle is impaired in people with Parkinson's Disease. *Movement Disorders: Clinical Practice* 2017;4(4): 524-528
7. Paul S, Sherrington C, Canning C et al. The Relative Contribution of Physical and Cognitive Fall Risk Factors in People With Parkinson's Disease: A Large Prospective Cohort Study *Neurorehabilitation and Neural Repair* 2014, Vol. 28(3) 282– 290
8. Konczak J, Sciutti A, Avanzino L, et al. Parkinson's disease accelerates age-related decline in haptic perception by altering somatosensory integration. *Brain* 2012;135;3371-3379.
9. Martens KA, Almeida QJ. Dissociating between sensory and perceptual deficits in PD: more than simply a motor deficit. *Mov Disord*. 2012 Mar;27(3):387-92
10. Pieruccini-Faria F, Martens K, Silveira C et al. Interactions between cognitive and sensory load while planning and controlling complex gait adaptations in Parkinson's disease. *BMC Neurology* 2014; 14:250
11. Vaugoyeau M, Hakam H, Azulay J-P. Proprioceptive impairment and postural orientation control in Parkinson's disease. *Human Movement Science* 2011;30;405-414
12. Connell L & Tyson S. Measures of sensation in neurological conditions; a systematic review. *Clin Rehabil* 2012; 26: 68
13. Stolk-Hornsveld F, Crow JL, Hendriks EP, van der Baan R and Harmeling-van der Wel BC. The Erasmus MC modifications to the (revised) Nottingham Sensory Assessment: a reliable somatosensory assessment measure for patients with intracranial disorders. *Clin Rehabil* 2006; 20: 160–72.
14. Fugl-Meyer AR, Jaasko L, Leynman I et al. The post-stroke hemiplegic patient: a method for evaluation of physical performance. *Scand J Rehabil Med* 1975; 7: 13-31
15. Borstad A & Nichols-Larsen D. Assessing and Treating Higher Level Somatosensory Impairments Post Stroke. *Topics in Stroke Rehabilitation* 2014; 21(4): 290-295
16. Gorst T, Rogers A, Morrison SC, Cramp M, Paton J, Freeman J & Marsden J. The prevalence, distribution, and functional importance of lower limb somatosensory impairments in chronic stroke survivors: a cross sectional observational study. *Disab Rehabil* 2018, DOI: 10.1080/09638288.2018.1468932
17. Carey L & Matyas T. Frequency of Discriminative Sensory Loss in the Hand after Stroke in a Rehabilitation Setting. *J Rehabil Med* 2011; 43: 257–263

18. Hilier S, Immink M, Thewlis D. Assessing proprioception: A Systematic Review of Possibilities. *Neurorehabil and Neural Repair* 2015; 29(10): 933–949
19. Gorst T, Freeman J, Yarrow K and Marsden J. (2019a) Assessing plantar tactile sensation in stroke using the FoRDT™: a reliability and validity study. *PM&R* : DOI: 10.1002/pmrj.12085
20. Gorst T, Freeman J, Yarrow K, Marsden J. (2019b) Assessing lower limb position sense in stroke using the GradDT™ and StepDT™: a reliability and validity study. *Disability and Rehabil*: doi 10.1080/09638288.2018.1554008
21. Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12:189-198
22. Shoukri M, Asayli M, Donner A. Sample size requirements for the design of reliability study: review and new results. *Statistical Methods in Medical Research* 2004; 13: 1:21
23. Goetz C, Tilley B, Shaftmann S et al. Movement Disorder Society-Sponsored Revision of the Unified Parkinson’s Disease Rating Scale (MDS-UPDRS): Scale Presentation and Clinimetric Testing Results *Movement Disorders* 2008; 23(15):2129–2170
24. Leek M. Adaptive procedures in psychophysical research. *Perception & Psychophysics* 2001, 63 (8), 1279-1292
25. Morley J, Goodwin A, Darians Smith I. Tactile Discrimination of gratings. *Experimental Brain Research* 1983; 49(2): 291-299
26. Padgett P, Jacobs J, Kasser S. Is the BESTest at Its Best? A Suggested Brief Version Based on Interrater Reliability, Validity, Internal Consistency, and Theoretical Construct. *Physical Therapy*, 2012 92(9); 1197–1207
27. Horak F, Wrisley D, Frank J. The Balance Evaluation Systems Test (BESTest) to Differentiate Balance Deficits. *Physical Therapy* 2009: 89(5); 484–498
28. Duncan R, Leddy A, Cavanaugh J, Dibble L, Ellis T, Ford M, Foreman K, Earhart G. Comparative Utility of the BESTest, Mini-BESTest, and Brief-BESTest for Predicting Falls in Individuals With Parkinson Disease: A Cohort Study. *Physical Therapy*. 2013; 93(4); 542–550
29. Bohannon RW, Andrews AW, Thomas MW. Walking speed: reference values and correlates for older adults. *J Orthop Sports Phys Ther.* 1996;24(2):86-90
30. Bloem BR, Marinus J, Almeida Q, Dibble L, Nieuwboer A, Post B, Ruzicka E, Goetz C, Stebbins G, Martinez-Martin P, Schrag A, Movement Disorders Society Rating Scales. Measurement instruments to assess posture, gait, and balance in Parkinson’s disease: Critique and recommendations. *Mov Disord* 2016: 31:1343–1355
31. Fasano A, Canning C, Hausdorff J, Lord S, Rochester L. Falls in Parkinson’s Disease: A Complex and Evolving Picture. *Mov Disord* 2017;32 (11); 1524-1536.
32. Lamb SE, Jørstad-Stein EC, Hauer K, Becker C; Prevention of Falls Network Europe and Outcomes Consensus Group. Development of a common outcome data set for fall injury

- prevention trials: the Prevention of Falls Network Europe consensus *J Am Geriatr Soc* 2005 Sep;53(9):1618-22
33. Yardley, L., Beyer, N., Hauer, K., et al Development and initial validation of the Falls Efficacy Scale-International (FES-I). *Age and Ageing*, 2005; 34(6): 614-619.
 34. Kader M, Iwarsson S, Odin P, Nilsson MH. Fall-related activity avoidance in relation to a history of falls or near falls, fear of falling and disease severity in people with Parkinson's disease. *BMC Neurol*. 2016;16:84
 35. Kottner J, Audige L, Brorson S, et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. *Journal of Clinical Epidemiology* 2011; 64: 96-106
 36. Vaz S, Falkmer T, Passmore AE, Parsons R, Andreou P (2013) The Case for Using the Repeatability Coefficient When Calculating Test–Retest Reliability. *PLoS ONE* 8(9): e73990
 37. Pallant J. 2013 *SPSS Survival Manual*. 5th Edition. Maidenhead: Open University Press.
 38. Cohen J. (1988). *Statistical Power Analysis for the Behavioral Sciences*. New York, NY: Routledge Academic
 39. Conte A, Leodori G, Ferrazzano G, De Bartolo MI, Manzo N, Fabbrini G, et al. Somatosensory temporal discrimination threshold in Parkinson's disease parallels disease severity and duration. *Clin Neurophysiol* 2016;127:2985–9.
 40. Lee MS, Kim HS, Lyoo CH. “Off” gait freezing and temporal discrimination threshold in patients with Parkinson disease. *Neurology* 2005;64:670–4.
 41. Lee MS, Lee MJ, Conte A, Berardelli A. Abnormal somatosensory discrimination in Parkinson's disease: Pathophysiological correlates and the role in motor control deficits. *Clin Neurophysiol* 2018; 129; 442-447.
 42. Peterka RJ. Sensorimotor integration in human postural control. *J Neurophys* 2002; 88: 1097–1118
 43. Wolpert D, Pearson K & Ghez C. The Organization and planning of movement. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013. p. 743-767.
 44. Hwang S, Agad P, Grill S, Kiemel T Jeka J. A Central Processing Sensory Deficit with Parkinson's disease. *Exp Brain Res*. 2016; 234(8): 2369–2379
 45. Konczak J, Corcos D, Horak F, et al. Proprioception and motor control in Parkinson's Disease. *Journal of Motor Behaviour* 2009; 41:6; 543-552
 46. Robbe, D. To move or to sense? Incorporating somatosensory representation into striatal functions. *Current Opinion in Neurobiology* 2018, 52:123–130
 47. de Jong A, Kilbreath SL, Refshauge KM, Adams R. Performance in different proprioceptive tests does not correlate in ankles with recurrent sprain. *Arch Phys Med Rehabil* 2005;86:2101–2105.

- 501 48. McKeown MD, Peters R, Pasman E, McKeown MJ, Carpenter M, Inglis T. Plantar cutaneous
502 function in Parkinson's disease patients ON and OFF L-dopa. *Neuroscience Letters* 2016;
503 629: 251–255
- 504 49. Lord SR, Clark RD, Webster IW. Postural stability and associated physiological factors in a
505 population of aged persons. *J Gerontol* 1991; 46: 69–76
- 506 50. Lin S-I, Hsu L-J, Wang H-C. Effects of ankle proprioceptive interference on locomotion after
507 stroke. *Arch Phys Med Rehabil* 2012;93:1027-33
- 508 51. Bradford J, Lukos J, & Ferris D. Electrocortical activity distinguishes between uphill and
509 level walking in humans. *J Neurophysiol* 2016; 115:958-966
- 510 52. Sipp AR, Gwin JT, Makeig S, Ferris DP. Loss of balance during balance beam walking elicits
511 a multifocal theta band electrocortical response. *J Neurophysiol* 110: 2050 –2060, 2013
- 512 53. Barker, R.A. & Williams-Gray, C.H. (2015) Mild cognitive impairment and Parkinson's
513 disease-something to remember. *J. Parkinsons Dis.*, 4, 651–656.
- 514 54. Stocchi F, Abbruzzese G, Ceravolo R, et al. Prevalence of fatigue in Parkinson disease and its
515 clinical correlates. *Neurology* 2014;83:215–220

Table 1. PD and control participant demographic and clinical characteristics

Characteristics	PD (n=27)	Control (n=27)
Age, years, mean (SD)	71 (5.8)	70 (7.0)
Gender n (%)		
Male	19 (70.4)	17 (62.9)
Female	8 (29.6)	10 (37.1)
Time since diagnosis, years mean (SD)	5.7 (4.9)	-
Hoehn & Yahr stage, n (%)		
1	3 (11.1)	-
2	14 (51.9)	-
3	9 (33.3)	-
4	1 (3.7)	-
MDS-UPDRS Score, mean (SD)	30.1 (14.7)	
Number of falls reported n (%)		
0	12 (44.4)	20 (74)
1	3 (11.1)	4 (15)
2	2 (7.4)	3 (11)
3	4 (14.8)	0
>4	6 (22.3)	0

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Table 2. Intra-rater reliability of novel sensory measures

Measure	<i>Intra-rater Reliability (Parkinson's n=27)</i>					
	Test 1 (T1)	Test 2 (T2)	Mean (T1 &T2)	SEM	ICC _(2,1) (95% CI)	CoR
GradDT™ threshold degrees (°) mean (SD)	2.4 (1.2)	2.2 (1.0)	2.3 (1.1)	0.31	0.92 (0.82-0.96)*	0.85
FoRDT™ threshold µm, mean (SD)	480 (240)	520 (210)	500 (235)	124	0.72 (0.38-0.87)*	340
StepDT™ threshold cm mean (SD)	1.8 (0.9)	1.9 (0.7)	1.8 (0.7)	0.36	0.73 (0.40-0.88)*	1.0

Abbreviations: GradDT, Gradient Discrimination Test; StepDT, Step-height Discrimination Test; FoRDT, Foot Roughness Discrimination Test; cm, centimetres; SD, Standard Deviation; SEM, Standard error of measurement; ICC(2,1) Intraclass Correlation Coefficient model 2,1; CI, Confidence Interval; CoR, Coefficient of Repeatability
*P<0.001

Table 3. Comparison of sensory performance between people with Parkinson's disease (PD) and healthy control group

Sensory Measure	PD (n=27)	Control (N=27)	p	Effect Size <i>d</i>
GradDT™ threshold degrees (°) Median (IQR, range)	2.5° (1.75°, 5.5°)	1.4° (1.1°, 2.5°)	<0.001	0.52
FoRDT™ threshold µm Median (IQR, range)	400 (400, 900)	300 (325, 850)	0.22	0.16
StepDT™ threshold cm Median (IQR, range)	1.8 (1.2, 3.0)	1.2 (0.6, 1.8)	0.001	0.47
EmNSA score, median (IQR, range)				
Tactile Sensation (0-64)	64 (7,15)	62 (4,13)	0.59	0.07
Proprioception score (0-16)	16 (0, 2)	16 (0,2)	0.31	0.13

Abbreviations: GradDT, Gradient Discrimination Test; StepDT, Step-height Discrimination Test; FoRDT, Foot Roughness Discrimination Test; EmNSA, Erasmus modified version of Nottingham Sensory Assessment; cm, centimetres; SD, Standard Deviation; µm, micrometres; *d* Cohen's *d*.

Table 4. Spearman rank order correlation coefficients between novel measures and Erasmus MC modified Nottingham Sensory Assessment

*p<0.05
Abbreviations: EmNSA, Erasmus MC modified Nottingham Sensory Assessment; GradDT™, Gradient Discrimination Test; StepDT™, Step Height Discrimination Test; FoRDT™, Foot Roughness Discrimination Test

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592 Table 5. Spearman rank order correlation coefficients between sensory measures and functional
 593 mobility measures

Sensory Measure	Falls Incidence	Falls Efficacy Scale -I	Brief BESTest	Gait Speed m/s	Step length
GradDT	0.55**	0.44*	- 0.63**	0.20	0.06
StepDT	0.24	0.1	- 0.54**	0.12	0.09
FoRDT	0.03	0.15	-0.11	-0.17	0.05
EmNSA (Tactile)	-0.21	-0.37	0.17	0.03	0.02
EmNSA (Proprioception)	0.15	-0.37	-0.31	0.15	0.17

*p<0.05; **P,0.01; Abbreviations: GradDT, Gradient Discrimination Test; StepDT, Step height discrimination test; FoRDT, foot roughness discrimination test; EmNSA, Erasmus MC modified Nottingham Sensory Assessment; FES-I, Falls Efficacy Scale – International; BriefBESTest, Brief version of Balance Evaluations Systems Test;

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